paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Title:

Please substitute the following Title of the Invention for the pending Title of the Invention:

A COMPOSITION COMPRISING A METAL CHELATOR AND A METHOD OF TREATING AMYLOIDOSIS BY ADMINISTERING THE METAL CHELATOR

In the Specification:

Cross-Reference to Related Applications:

On page 1, immediately after the title, please insert the following caption and paragraph:

CROSS REFERENCE TO RELATED APPLICATIONS

C1

This application is a 371 of PCT/US98/04683, filed March 11, 1998 and published under PCT Article 21(2) in English on September 17, 1998, which claims the benefit of the filing date of U.S. Patent Application No. 08/816,122, filed March 11, 1997, now abandoned.

Description of the Figures:

On page 19, please replace the paragraph that beings on line 3 and ends on line 5 with the following:

C2

Figure 6 shows the amino acid sequence of $APP_{669-716}$ near $A\beta_{1-42}$ (SEQ ID NO:1). Rat Aβ is mutated (R5G, Y10F, H13R; bold). Possible metal-binding residues are underlined.

On page 21, please replace the paragraph that begins on line 21 and ends on line 24 with the following:

C3

Figures 19A, 19C and 19E show the results of Western blot analysis of 6 AD brain samples homogenized in the presence of chelators as indicated. Figures 19B and 19D show the results of densitometry analysis of the Western blots of Figs. 19A and 19C, respectively. Figures 19A-19E show that metal chelators promote the solubilization of Aβ from human brain sample homogenates.

On page 22, please replace the paragraph that begins on line 19 and ends on line 25 with the following:

C4

Figures 26A and 26B show that chelation promotes the solubilization of $A\beta_{1-40}$ and $A\beta_{1-42}$ from AD and non-AD tissue. Representative AD (Fig. 26A) and aged-matched control specimens (Fig. 26B) were prepared as described in PBS or 5 mM BC. Identical gels were run and Western blots

C4

were probed with mAbs WO2 (raised against residues 5-16, recognizes $A\beta_{1-40}$ and $A\beta_{1-42}$) G210 (raised against residues 35-40, recognizes $A\beta_{1-40}$) or G211 (raised against residues 35-42, recognizes $A\beta_{1-42}$) (See Ida, N. *et al.*, *J. Biol. Chem.* *271*:22908 1996).

On page 23, please replace the paragraph that begins on line 13 and ends on line 28 with the following:

C5

Figures 30A-30E show dissolution of SDS-resistant Aβ polymers. Figures 30A-1 and 30A-2 show that chaotrophic agents are unable to disrupt polymerization. Figure 30B shows that metal ion chelators disrupt SDS-resistant $A\beta_{1-40}$ polymers. Figure 30C shows that metal ion chelators disrupt SDS-resistant $A\beta_{1-42}$ polymers. The chelators, their log stability constant, and their molecular weight, respectively, are as follows: TETA (tetraethylenediamine), 20.4, 146; EDTA (ethylenediaminetetra acetic acid), 18.1, 292; DTPA (diethylenetriaminopenta acetic acid), 21.1, 393; CDTA (*trans*-1,2-diaminocyclohexanetetra acetic acid), 22.0, 346; and NTA (nitrilotriacetic acid), 13.1, 191. Figure 30D shows that α-helical promoting solvents and low pH disrupt polymers. Aliquots of $A\beta_{1-42}$ were incubated at pH 1 or with DMSO/HFIP (75%:25%) for 2 h (30 min., 37°C). Figure 30E shows that metal ion chelators disrupt SDS-resistant Aβ polymers extracted from AD brains. Aliquots of SDS-resistant Aβ polymers extracted from AD brains were incubated with no chelator, TETA (1 mM or 5 mM) or BC (1